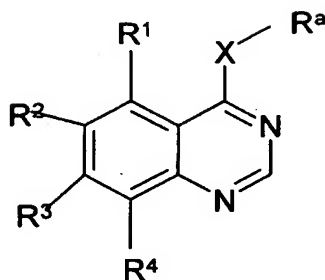


Claims

1. The use of a compound of formula (I)

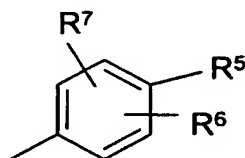


(I)

or a salt, ester, amide or prodrug thereof;

where X is O, or S, S(O) or S(O)₂, NH or NR⁸ where R⁸ is hydrogen or C₁₋₆alkyl;

R^a is a 3-quinoline group or a group of sub-formula (i)



(i)

where R⁵ is either a group -Z-(CH₂)_n-R⁹, halogen, a group of formula NR¹⁰R^{10'}, an optionally substituted hydrocarbyl group (other than ethenyl substituted by a carboxy group or an amide or sulphonamide derivative thereof), an optionally substituted heterocyclyl group or an optionally substituted alkoxy group; where Z is O or S, n is 0, or an integer of from 1 to 6, R⁹ is hydrogen or optionally substituted hydrocarbyl or optionally substituted heterocyclyl; R¹⁰ and R^{10'} are independently selected from hydrogen, optionally substituted hydrocarbyl or optionally substituted heterocyclyl, or R¹⁰ and R^{10'} together with the nitrogen atom to which they are attached form an optionally substituted heterocyclic ring which may optionally contain further heteroatoms, or an azo group of formula -N=N-R¹¹ where R¹¹ is an optionally substituted hydrocarbyl group or optionally substituted heterocyclyl group;

R^6 and R^7 are independently selected from hydrogen, halo, C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} alkoxymethyl, di(C_{1-4} alkoxy)methyl, C_{1-4} alkanoyl, trifluoromethyl, cyano, amino, C_{2-5} alkenyl, C_{2-5} alkynyl, a phenyl group, a benzyl group or a 5-6-membered heterocyclic group with 1-3 heteroatoms, selected independently from O, S and N, which heterocyclic group may be aromatic or non-aromatic and may be saturated (linked via a ring carbon or nitrogen atom) or unsaturated (linked via a ring carbon atom), and which phenyl, benzyl or heterocyclic group may bear on one or more ring carbon atoms up to 5 substituents selected from hydroxy, halogeno, C_{1-3} alkyl, C_{1-3} alkoxy, C_{1-3} alkanoyloxy, trifluoromethyl, cyano, amino, nitro, C_{2-4} alkanoyl, C_{1-4} alkanoylamino, C_{1-4} alkoxycarbonyl, C_{1-4} alkylsulphanyl, C_{1-4} alkylsulphinyl, C_{1-4} alkylsulphonyl, carbamoyl, N - C_{1-4} alkylcarbamoyl, N,N -di(C_{1-4} alkyl)carbamoyl, aminosulphonyl, N - C_{1-4} alkylaminosulphonyl, N,N -di(C_{1-4} alkyl)aminosulphonyl, C_{1-4} alkylsulphonylamino, and a saturated heterocyclic group selected from morpholino, thiomorpholino, pyrrolidinyl, piperazinyl, piperidinyl imidazolidinyl and pyrazolidinyl, which saturated heterocyclic group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno, C_{1-3} alkyl, C_{1-3} alkoxy, C_{1-3} alkanoyloxy, trifluoromethyl, cyano, amino, nitro and C_{1-4} alkoxycarbonyl, and

R^1 , R^2 , R^3 , R^4 are independently selected from halogeno, cyano, nitro, C_{1-3} alkylsulphanyl, $-N(OH)R^{12}$ (wherein R^{12} is hydrogen, or C_{1-3} alkyl), or $R^{14}X^1$ - (wherein X^1 represents a direct bond, $-O-$, $-CH_2-$, $-OC(O)-$, $-C(O)-$, $-S-$, $-SO-$, $-SO_2-$, $-NR^{15}C(O)-$, $-C(O)NR^{16}-$, $-SO_2NR^{17}-$, $-NR^{18}SO_2-$ or $-NR^{19}-$ (wherein R^{15} , R^{16} , R^{17} , R^{18} and R^{19} each independently represents hydrogen, C_{1-3} alkyl or C_{1-3} alkoxy C_{2-3} alkyl), and R^{14} is hydrogen, optionally substituted hydrocarbyl, optionally substituted heterocyclyl or optionally substituted alkoxy; in the preparation of a medicament for use in the inhibition of aurora 2 kinase.

2. The use according to claim 1 wherein in the compound of formula (I), at least one group R^1 , R^2 , R^3 , R^4 is a group $R^{14}X^1$ - and R^{14} is hydrogen, an optionally substituted hydrocarbyl group selected from alkyl, alkenyl, alkynyl, aryl, aralkyl, cycloalkyl, cycloalkenyl or cycloalkynyl, or combinations thereof; or an

optionally substituted heterocyclyl group of from 4 to 20 ring atoms, at least one of which is a heteroatom such as oxygen, sulphur or nitrogen and where the optional substituents comprise at least one functional group selected from nitro, cyano, halo, oxo, $=CR^{78}R^{79}$, $C(O)_xR^{77}$, OR^{77} , $S(O)_yR^{77}$, $NR^{78}R^{79}$, $C(O)NR^{78}R^{79}$, $OC(O)NR^{78}R^{79}$, $=NOR^{77}$, $-NR^{77}C(O)_xR^{78}$, $-NR^{77}CONR^{78}R^{79}$, $-N=CR^{78}R^{79}$, $S(O)_yNR^{78}R^{79}$ or $-NR^{77}S(O)_yR^{78}$ where R^{77} , R^{78} and R^{79} are independently selected from hydrogen, optionally substituted hydrocarbyl, optionally substituted heterocyclyl or optionally substituted alkoxy, or R^{78} and R^{79} together form an optionally substituted ring which optionally contains further heteroatoms such as oxygen, nitrogen, S, $S(O)$ or $S(O)_2$, where x is an integer of 1 or 2, y is 0 or an integer of 1-3.

3. The use according to claim 2 where hydrocarbyl, heterocyclyl or alkoxy groups R^{77} , R^{78} and R^{79} as well as rings formed by R^{78} and R^{79} are optionally substituted by halo, perhaloalkyl, mercapto, alkylthio, hydroxy, carboxy, alkoxy, heteroaryl, heteroaryloxy, cycloalkyl, cycloalkenyl, cycloalkynyl, alkenyloxy, alkynyloxy, alkoxyalkoxy, aryloxy (where the aryl group may be substituted by halo, nitro, or hydroxy), cyano, nitro, amino, mono- or di-alkyl amino, oximino or $S(O)_yR^{90}$ where y is as defined above and R^{90} is an alkyl.
4. The use according to any one of the preceding claims where in the compound of formula (I) at least one of R^1 , R^2 , R^3 and R^4 is a group $R^{14}X^1$ - where X^1 is as defined in relation to formula (I) and R^{14} is selected from one of the following twenty-two groups:
 - 1) hydrogen or C_{1-5} alkyl which may be unsubstituted or which may be substituted with one or more functional groups;
 - 2) $-R^aX^2C(O)R^{20}$ (wherein X^2 represents -O- or $-NR^{21}$ - (in which R^{21} represents hydrogen, or alkyl optionally substituted with a functional group) and R^{20} represents C_{1-3} alkyl, $-NR^{22}R^{23}$ or $-OR^{24}$ (wherein R^{22} , R^{23} and R^{24} which may be the same or different each represents hydrogen, or alkyl optionally substituted with a functional group);

- 3) $-R^bX^3R^{25}$ (wherein X^3 represents $-O-$, $-C(O)-$, $-S-$, $-SO-$, $-SO_2-$, $-OC(O)-$, $-NR^{26}C(O)-$, $-NR^{26}C(O)O-$, $-C(O)NR^{27}-$, $-C(O)ONR^{27}-$, $-SO_2NR^{28}-$, $-NR^{29}SO_2-$ or $-NR^{30}-$ (wherein R^{26} , R^{27} , R^{28} , R^{29} and R^{30} each independently represents hydrogen, or alkyl optionally substituted with a functional group) and R^{25} represents hydrogen, hydrocarbyl (as defined herein) or a saturated heterocyclic group, wherein the hydrocarbyl or heterocyclic groups may be optionally substituted by one or more functional groups and the heterocyclic groups may additionally be substituted by a hydrocarbyl group;
- 4) $-R^cX^4R^{c'}X^5R^{31}$ (wherein X^4 and X^5 which may be the same or different are each $-O-$, $-C(O)-$, $-S-$, $-SO-$, $-SO_2-$, $-OC(O)-$, $-NR^{32}C(O)-$, $-NR^{32}C(O)O-$, $-C(O)NR^{33}-$, $-C(O)ONR^{33}-$, $-SO_2NR^{34}-$, $-NR^{35}SO_2-$ or $-NR^{36}-$ (wherein R^{32} , R^{33} , R^{34} , R^{35} and R^{36} each independently represents hydrogen or alkyl optionally substituted by a functional group) and R^{31} represents hydrogen, or alkyl optionally substituted by a functional group;
- 5) R^{37} wherein R^{37} is a C_{3-6} cycloalkyl or saturated heterocyclic ring (linked via carbon or nitrogen), which cycloalkyl or heterocyclic group may be substituted by one or more functional groups or by a hydrocarbyl or heterocyclyl group which hydrocarbyl or heterocyclyl group may be optionally substituted by one or more functional groups;
- 6) $-R^dR^{37}$ (wherein R^{37} is as defined hereinbefore);
- 7) $-R^eR^{37}$ (wherein R^{37} is as defined hereinbefore);
- 8) $-R^fR^{37}$ (wherein R^{37} is as defined hereinbefore);
- 9) R^{38} (wherein R^{38} represents a pyridone group, an aryl group or an aromatic heterocyclic group (linked via carbon or nitrogen) with 1-3 heteroatoms selected from O, N and S, which pyridone, aryl or aromatic heterocyclic group may be substituted by one or more functional groups or by a hydrocarbyl group optionally substituted by one or more functional groups or heterocyclyl groups, or by a heterocyclyl group optionally substituted by one or more functional groups or hydrocarbyl groups);
- 10) $-R^gR^{38}$ (wherein R^{38} is as defined hereinbefore);
- 11) $-R^hR^{38}$ (wherein R^{38} is as defined hereinbefore);
- 12) $-R^iR^{38}$ (wherein R^{38} is as defined hereinbefore);

- 13) $-R^j X^6 R^{38}$ (wherein X^6 represents $-O-$, $-S-$, $-SO-$, $-SO_2-$, $-OC(O)-$, $-NR^{43}C(O)-$, $-NR^{43}C(O)O-$, $-C(O)NR^{44}-$, $-C(O)ONR^{44}-$, $-SO_2NR^{45}-$, $-NR^{46}SO_2-$ or $-NR^{47}-$ (wherein R^{43} , R^{44} , R^{45} , R^{46} and R^{47} each independently represents hydrogen, or alkyl optionally substituted with a functional group) and R^{38} is as defined hereinbefore);
- 14) $-R^k X^7 R^{38}$ (wherein X^7 represents $-O-$, $-C(O)-$, $-S-$, $-SO-$, $-SO_2-$, $-OC(O)-$, $-NR^{48}C(O)-$, $-NR^{48}C(O)O-$, $-C(O)NR^{49}-$, $-C(O)ONR^{49}-$, $-SO_2NR^{50}-$, $-NR^{51}SO_2-$ or $-NR^{52}-$ (wherein R^{48} , R^{49} , R^{50} , R^{51} and R^{52} each independently represents hydrogen, or alkyl optionally substituted with a functional group) and R^{38} is as defined hereinbefore);
- 15) $-R^m X^8 R^{38}$ (wherein X^8 represents $-O-$, $-C(O)-$, $-S-$, $-SO-$, $-SO_2-$, $-OC(O)-$, $-NR^{53}C(O)-$, $-NR^{53}C(O)O-$, $-C(O)NR^{54}-$, $-C(O)ONR^{54}-$, $-SO_2NR^{55}-$, $-NR^{56}SO_2-$ or $-NR^{57}-$ (wherein R^{53} , R^{54} , R^{55} , R^{56} and R^{57} each independently represents hydrogen, or alkyl optionally substituted with a functional group) and R^{38} is as defined hereinbefore);
- 16) $-R^n X^9 R^{38}$ (wherein X^9 represents $-O-$, $-C(O)-$, $-S-$, $-SO-$, $-SO_2-$, $-OC(O)-$, $-NR^{58}C(O)-$, $-NR^{58}C(O)O-$, $-C(O)NR^{59}-$, $-C(O)ONR^{59}-$, $-SO_2NR^{60}-$, $-NR^{61}SO_2-$ or $-NR^{62}-$ (wherein R^{58} , R^{59} , R^{60} , R^{61} and R^{62} each independently represents hydrogen, or alkyl optionally substituted with a functional group) and R^{38} is as defined hereinbefore);
- 17) $-R^p X^9 -R^{p'} R^{37}$ (wherein X^9 and R^{37} are as defined hereinbefore);
- 18) C_{2-5} alkenyl which may be unsubstituted or which may be substituted with one or more functional groups;
- 19) C_{2-5} alkynyl which may be unsubstituted or which may be substituted with one or more functional groups;
- 20) $-R^t X^9 R^{t'} R^{37}$ (wherein X^9 and R^{37} are as defined hereinbefore);
- 21) $-R^u X^9 R^{u'} R^{37}$ (wherein X^9 and R^{37} are as defined hereinbefore); and
- 22) $-R^v R^{63} (R^{v'})_q (X^9)_r R^{64}$ (wherein X^9 is as defined hereinbefore, q is 0 or 1, r is 0 or 1, and R^{63} is a C_{1-3} alkylene group or a cyclic group selected from divalent cycloalkyl or heterocyclic group, which C_{1-3} alkylene group may be substituted by one or more functional groups and which cyclic group may be substituted by one or more functional groups or by a hydrocarbonyl group optionally substituted by

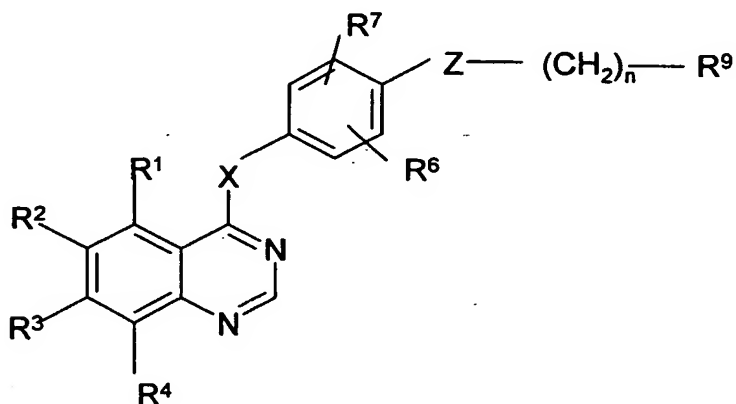
one or more functional groups or heterocyclyl groups, or by a heterocyclyl group optionally substituted by one or more functional groups or hydrocarbyl groups; and R^{64} is hydrogen, C_{1-3} alkyl, or a cyclic group selected from cycloalkyl or heterocyclic group, which C_{1-3} alkyl group may be substituted by one or more functional groups and which cyclic group may be substituted by one or more may be substituted by one or more functional groups or by a hydrocarbyl group optionally substituted by one or more functional groups or heterocyclyl groups, or by a heterocyclyl group optionally substituted by one or more functional groups or hydrocarbyl groups;

and wherein $R^a, R^b, R^c, R^d, R^e, R^f, R^g, R^h, R^i, R^j, R^k, R^l, R^m, R^n, R^o, R^p, R^q, R^r, R^s, R^t, R^u, R^v$ and R^w are independently selected from C_{1-8} alkylene groups optionally substituted by one or more functional groups,

R^e, R^h, R^k and R^l are independently selected from C_{2-8} alkenylene groups optionally substituted by one or more functional groups, and

R^f, R^i, R^m and R^u are independently selected from C_{2-8} alkynylene groups optionally substituted by one or more functional groups.

5. The use according to any one of the preceding claims wherein the compound of formula (I) is a compound of formula (II)



(II)

or a salt, ester, amide or prodrug thereof;

where $X, Z, n, R^9, R^6, R^7, R^1, R^2, R^3$ and R^4 are as defined in claim 1.

6. The use according to claim 5 wherein the compound of formula (II) is compound of formula (IIA) which has the structure (II) as shown in claim 5, or a salt, ester or amide thereof; and
- where X is O, or S, S(O) or S(O)₂, or NR⁸ where R⁸ is hydrogen or C₁₋₆alkyl;
- Z is O or S,
- n is 0, or an integer of from 1 to 6
- R⁹ is hydrogen or optionally substituted hydrocarbyl or optionally substituted heterocyclyl;
- and R⁶ and R⁷ are independently selected from hydrogen, halo, C₁₋₄alkyl, C₁₋₄alkoxy, C₁₋₄alkoxymethyl, di(C₁₋₄alkoxy)methyl, C₁₋₄alkanoyl, trifluoromethyl, cyano, amino, C₂₋₅alkenyl, C₂₋₅alkynyl, a phenyl group, a benzyl group or a 5-6-membered heterocyclic group with 1-3 heteroatoms, selected independently from O, S and N, which heterocyclic group may be aromatic or non-aromatic and may be saturated (linked via a ring carbon or nitrogen atom) or unsaturated (linked via a ring carbon atom), and which phenyl, benzyl or heterocyclic group may bear on one or more ring carbon atoms up to 5 substituents selected from hydroxy, halogeno, C₁₋₃alkyl, C₁₋₃alkoxy, C₁₋₃alkanoyloxy, trifluoromethyl, cyano, amino, nitro, C₂₋₄alkanoyl, C₁₋₄alkanoylamino, C₁₋₄alkoxycarbonyl, C₁₋₄alkylsulphanyl, C₁₋₄alkylsulphinyl, C₁₋₄alkylsulphonyl, carbamoyl, N-C₁₋₄alkylcarbamoyl, N,N-di(C₁₋₄alkyl)carbamoyl, aminosulphonyl, N-C₁₋₄alkylaminosulphonyl, N,N-di(C₁₋₄alkyl)aminosulphonyl, C₁₋₄alkylsulphonylamino, and a saturated heterocyclic group selected from morpholino, thiomorpholino, pyrrolidinyl, piperazinyl, piperidinyl, imidazolidinyl and pyrazolidinyl, which saturated heterocyclic group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno, C₁₋₃alkyl, C₁₋₃alkoxy, C₁₋₃alkanoyloxy, trifluoromethyl, cyano, amino, nitro and C₁₋₄alkoxycarbonyl, and
- R¹, R², R³, R⁴ are independently selected from, halo, cyano, nitro, trifluoromethyl, C₁₋₃alkyl, -NR¹²R¹³ (wherein R¹² and R¹³, which may be the same or different, each represents hydrogen or C₁₋₃alkyl), or -X¹R¹⁴ (wherein X¹ represents a direct bond, -O-, -CH₂-, -OCO-, carbonyl, -S-, -SO-, -SO₂-, -NR¹⁵CO-, -CONR¹⁶-, -SO₂NR¹⁷-, -NR¹⁸SO₂- or -NR¹⁹- (wherein R¹⁵, R¹⁶, R¹⁷,

R^{18} and R^{19} each independently represents hydrogen, C_{1-3} alkyl or C_{1-3} alkoxy C_{2-3} alkyl), and R^{14} is selected from one of the following groups:

- 1') hydrogen or C_{1-5} alkyl which may be unsubstituted or which may be substituted with one or more groups selected from hydroxy, fluoro or amino,
- 2') C_{1-5} alkyl X^2COR^{20} (wherein X^2 represents -O- or - NR^{21} - (in which R^{20} represents hydrogen, C_{1-3} alkyl or C_{1-3} alkoxy C_{2-3} alkyl) and R^{21} represents C_{1-3} alkyl, - $NR^{22}R^{23}$ or - OR^{24} (wherein R^{22} , R^{23} and R^{24} which may be the same or different each represents hydrogen, C_{1-3} alkyl or C_{1-3} alkoxy C_{2-3} alkyl);
- 3') C_{1-5} alkyl X^3R^{25} (wherein X^3 represents -O-, -S-, -SO-, -SO₂-, -OCO-, - $NR^{26}CO$ -, -CONR²⁷-, -SO₂NR²⁸-, -NR²⁹SO₂- or -NR³⁰- (wherein R^{26} , R^{27} , R^{28} , R^{29} and R^{30} each independently represents hydrogen, C_{1-3} alkyl or C_{1-3} alkoxy C_{2-3} alkyl) and R^{25} represents hydrogen, C_{1-3} alkyl, cyclopentyl, cyclohexyl or a 5-6-membered saturated heterocyclic group with 1-2 heteroatoms, selected independently from O, S and N, which C_{1-3} alkyl group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno and C_{1-4} alkoxy and which cyclic group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno, C_{1-4} alkyl, C_{1-4} hydroxyalkyl and C_{1-4} alkoxy);
- 4') C_{1-5} alkyl X^4C_{1-5} alkyl X^5R^{31} (wherein X^4 and X^5 which may be the same or different are each -O-, -S-, -SO-, -SO₂-, -NR³²CO-, -CONR³³-, -SO₂NR³⁴-, -NR³⁵SO₂- or -NR³⁶- (wherein R^{32} , R^{33} , R^{34} , R^{35} and R^{36} each independently represents hydrogen, C_{1-3} alkyl or C_{1-3} alkoxy C_{2-3} alkyl) and R^{31} represents hydrogen or C_{1-3} alkyl);
- 5') R^{37} (wherein R^{37} is a 5-6-membered saturated heterocyclic group (linked via carbon or nitrogen) with 1-2 heteroatoms, selected independently from O, S and N, which heterocyclic group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno, C_{1-4} alkyl, C_{1-4} hydroxyalkyl, C_{1-4} alkoxy, C_{1-4} alkoxy C_{1-4} alkyl and C_{1-4} alkylsulphonyl C_{1-4} alkyl);
- 6') C_{1-5} alkyl R^{37} (wherein R^{37} is as defined hereinbefore in (5'));
- 7') C_{2-5} alkenyl R^{37} (wherein R^{37} is as defined hereinbefore in (5'));
- 8') C_{2-5} alkynyl R^{37} (wherein R^{37} is as defined hereinbefore in (5'));
- 9') R^{38} (wherein R^{38} represents a pyridone group, a phenyl group or a 5-6-membered aromatic heterocyclic group (linked via carbon or nitrogen) with

1-3 heteroatoms selected from O, N and S, which pyridone, phenyl or aromatic heterocyclic group may carry up to 5 substituents on an available carbon atom selected from hydroxy, halogeno, amino, C₁₋₄alkyl, C₁₋₄alkoxy, C₁₋₄hydroxyalkyl, C₁₋₄aminoalkyl, C₁₋₄alkylamino, C₁₋₄hydroxyalkoxy, carboxy, trifluoromethyl, cyano, -CONR³⁹R⁴⁰ and -NR⁴¹COR⁴² (wherein R³⁹, R⁴⁰, R⁴¹ and R⁴², which may be the same or different, each represents hydrogen, C₁₋₄alkyl or C₁₋₃alkoxyC₂₋₃alkyl));

10') C₁₋₅alkylR³⁸ (wherein R³⁸ is as defined hereinbefore in (9'));

11') C₂₋₅alkenylR³⁸ (wherein R³⁸ is as defined hereinbefore in (9'));

12') C₂₋₅alkynylR³⁸ (wherein R³⁸ is as defined hereinbefore in (9'));

13') C₁₋₅alkylX⁶R³⁸ (wherein X⁶ represents -O-, -S-, -SO-, -SO₂-, -NR⁴³CO-, -CONR⁴⁴-, -SO₂NR⁴⁵-, -NR⁴⁶SO₂- or -NR⁴⁷- (wherein R⁴³, R⁴⁴, R⁴⁵, R⁴⁶ and R⁴⁷ each independently represents hydrogen, C₁₋₃alkyl or C₁₋₃alkoxyC₂₋₃alkyl) and R³⁸ is as defined hereinbefore in (9'));

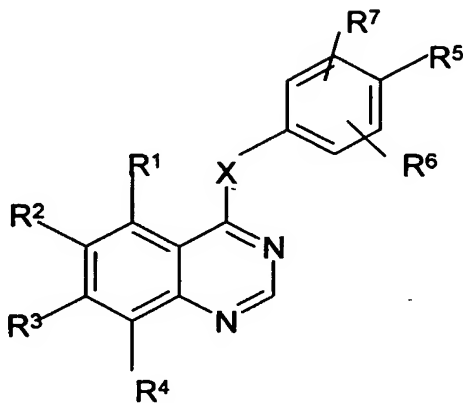
14') C₂₋₅alkenylX⁷R³⁸ (wherein X⁷ represents -O-, -S-, -SO-, -SO₂-, -NR⁴⁸CO-, -CONR⁴⁹-, -SO₂NR⁵⁰-, -NR⁵¹SO₂- or -NR⁵²- (wherein R⁴⁸, R⁴⁹, R⁵⁰, R⁵¹ and R⁵² each independently represents hydrogen, C₁₋₃alkyl or C₁₋₃alkoxyC₂₋₃alkyl) and R³⁸ is as defined hereinbefore in (9'));

15') C₂₋₅alkynylX⁸R³⁸ (wherein X⁸ represents -O-, -S-, -SO-, -SO₂-, -NR⁵³CO-, -CONR⁵⁴-, -SO₂NR⁵⁵-, -NR⁵⁶SO₂- or -NR⁵⁷- (wherein R⁵³, R⁵⁴, R⁵⁵, R⁵⁶ and R⁵⁷ each independently represents hydrogen, C₁₋₃alkyl or C₁₋₃alkoxyC₂₋₃alkyl) and R³⁸ is as defined hereinbefore in (9'));

16') C₁₋₃alkylX⁹C₁₋₃alkylR³⁸ (wherein X⁹ represents -O-, -S-, -SO-, -SO₂-, -NR⁵⁸CO-, -CONR⁵⁹-, -SO₂NR⁶⁰-, -NR⁶¹SO₂- or -NR⁶²- (wherein R⁵⁸, R⁵⁹, R⁶⁰, R⁶¹ and R⁶² each independently represents hydrogen, C₁₋₃alkyl or C₁₋₃alkoxyC₂₋₃alkyl) and R³⁸ is as defined hereinbefore in (9'));

17') C₁₋₃alkylX⁹C₁₋₃alkylR³⁷ (wherein X⁹ and R³⁷ are as defined hereinbefore in (5')).

7. The use according to any one of claims 1 to 5 wherein the compound of formula (I) is a compound of formula (III)



(III)

or a salt, ester, amide or prodrug thereof;

where X, R¹, R², R³, R⁴, R⁶ and R⁷ are as defined in claim 1 and R^{5'} is an optionally substituted hydrocarbyl, optionally substituted heterocyclyl or optionally substituted alkoxy group, provided that R^{5'} is other than ethenyl substituted by a carboxy group or an amide or sulphonamide derivative thereof.

8. The use according to claim 7 wherein the compound of formula (III) is a compound of formula (IIIA) which is of structure (III) as shown above, or a salt, ester or amide thereof; and
- where X is O, or S, S(O) or S(O)₂, or NR⁸ where R⁸ is hydrogen or C₁₋₆alkyl; R^{5'} is hydrogen or optionally substituted hydrocarbyl or optionally substituted heterocyclyl;
- and R⁶ and R⁷ are independently selected from hydrogen, halo, C₁₋₄alkyl, C₁₋₄alkoxy, C₁₋₄alkoxymethyl, di(C₁₋₄alkoxy)methyl, C₁₋₄alkanoyl, trifluoromethyl, cyano, amino, C₂₋₅alkenyl, C₂₋₅alkynyl, a phenyl group, a benzyl group or a 5-6-membered heterocyclic group with 1-3 heteroatoms, selected independently from O, S and N, which heterocyclic group may be aromatic or non-aromatic and may be saturated (linked via a ring carbon or nitrogen atom) or unsaturated (linked via a ring carbon atom), and which phenyl, benzyl or heterocyclic group may bear on one or more ring carbon atoms up to 5 substituents selected from hydroxy, halogeno, C₁₋₃alkyl, C₁₋₃alkoxy, C₁₋₃alkanoyloxy, trifluoromethyl,

cyano, amino, nitro, C₂₋₄alkanoyl, C₁₋₄alkanoylamino, C₁₋₄alkoxycarbonyl, C₁₋₄alkylsulphanyl, C₁₋₄alkylsulphinyl, C₁₋₄alkylsulphonyl, carbamoyl, N-C₁₋₄alkylcarbamoyl, N,N-di(C₁₋₄alkyl)carbamoyl, aminosulphonyl, N-C₁₋₄alkylaminosulphonyl, N,N-di(C₁₋₄alkyl)aminosulphonyl, C₁₋₄alkylsulphonylamino, and a saturated heterocyclic group selected from morpholino, thiomorpholino, pyrrolidinyl, piperazinyl, piperidinyl imidazolidinyl and pyrazolidinyl, which saturated heterocyclic group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno, C₁₋₃alkyl, C₁₋₃alkoxy, C₁₋₃alkanoyloxy, trifluoromethyl, cyano, amino, nitro and C₁₋₄alkoxycarbonyl, and

R¹, R², R³, R⁴ are independently selected from, halo, cyano, nitro, trifluoromethyl, C₁₋₃alkyl, -NR¹²R¹³ (wherein R¹² and R¹³, which may be the same or different, each represents hydrogen or C₁₋₃alkyl), or -X¹R¹⁴ (wherein X¹ represents a direct bond, -O-, -CH₂-, -OCO-, carbonyl, -S-, -SO-, -SO₂-, -NR¹⁵CO-, -CONR¹⁶-, -SO₂NR¹⁷-, -NR¹⁸SO₂- or -NR¹⁹- (wherein R¹⁵, R¹⁶, R¹⁷, R¹⁸ and R¹⁹ each independently represents hydrogen, C₁₋₃alkyl or C₁₋₃alkoxyC₂₋₃alkyl), and R¹⁴ is selected from one of the following groups:

- 1') hydrogen or C₁₋₅alkyl which may be unsubstituted or which may be substituted with one or more groups selected from hydroxy, fluoro or amino,
- 2') C₁₋₅alkylX²COR²⁰ (wherein X² represents -O- or -NR²¹- (in which R²⁰ represents hydrogen, C₁₋₃alkyl or C₁₋₃alkoxyC₂₋₃alkyl) and R²¹ represents C₁₋₃alkyl, -NR²²R²³ or -OR²⁴ (wherein R²², R²³ and R²⁴ which may be the same or different each represents hydrogen, C₁₋₃alkyl or C₁₋₃alkoxyC₂₋₃alkyl);
- 3') C₁₋₅alkylX³R²⁵ (wherein X³ represents -O-, -S-, -SO-, -SO₂-, -OCO-, -NR²⁶CO-, -CONR²⁷-, -SO₂NR²⁸-, -NR²⁹SO₂- or -NR³⁰- (wherein R²⁶, R²⁷, R²⁸, R²⁹ and R³⁰ each independently represents hydrogen, C₁₋₃alkyl or C₁₋₃alkoxyC₂₋₃alkyl) and R²⁵ represents hydrogen, C₁₋₃alkyl, cyclopentyl, cyclohexyl or a 5-6-membered saturated heterocyclic group with 1-2 heteroatoms, selected independently from O, S and N, which C₁₋₃alkyl group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno and C₁₋₄alkoxy and which cyclic group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno, C₁₋₄alkyl, C₁₋₄hydroxyalkyl and C₁₋₄alkoxy);

- 4') $C_{1-5}alkylX^4C_{1-5}alkylX^5R^{31}$ (wherein X^4 and X^5 which may be the same or different are each -O-, -S-, -SO-, -SO₂-, -NR³²CO-, -CONR³³-, -SO₂NR³⁴-, -NR³⁵SO₂- or -NR³⁶- (wherein R³², R³³, R³⁴, R³⁵ and R³⁶ each independently represents hydrogen, C₁₋₃alkyl or C₁₋₃alkoxyC₂₋₃alkyl) and R³¹ represents hydrogen or C₁₋₃alkyl);
- 5') R³⁷ (wherein R³⁷ is a 5-6-membered saturated heterocyclic group (linked via carbon or nitrogen) with 1-2 heteroatoms, selected independently from O, S and N, which heterocyclic group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno, C₁₋₄alkyl, C₁₋₄hydroxyalkyl, C₁₋₄alkoxy, C₁₋₄alkoxyC₁₋₄alkyl and C₁₋₄alkylsulphonylC₁₋₄alkyl);
- 6') C₁₋₅alkylR³⁷ (wherein R³⁷ is as defined hereinbefore in (5'));
- 7') C₂₋₅alkenylR³⁷ (wherein R³⁷ is as defined hereinbefore in (5'));
- 8') C₂₋₅alkynylR³⁷ (wherein R³⁷ is as defined hereinbefore in (5'));
- 9') R³⁸ (wherein R³⁸ represents a pyridone group, a phenyl group or a 5-6-membered aromatic heterocyclic group (linked via carbon or nitrogen) with 1-3 heteroatoms selected from O, N and S, which pyridone, phenyl or aromatic heterocyclic group may carry up to 5 substituents on an available carbon atom selected from hydroxy, halogeno, amino, C₁₋₄alkyl, C₁₋₄alkoxy, C₁₋₄hydroxyalkyl, C₁₋₄aminoalkyl, C₁₋₄alkylamino, C₁₋₄hydroxyalkoxy, carboxy, trifluoromethyl, cyano, -CONR³⁹R⁴⁰ and -NR⁴¹COR⁴² (wherein R³⁹, R⁴⁰, R⁴¹ and R⁴², which may be the same or different, each represents hydrogen, C₁₋₄alkyl or C₁₋₃alkoxyC₂₋₃alkyl);
- 10') C₁₋₅alkylR³⁸ (wherein R³⁸ is as defined hereinbefore in (9'));
- 11') C₂₋₅alkenylR³⁸ (wherein R³⁸ is as defined hereinbefore in (9'));
- 12') C₂₋₅alkynylR³⁸ (wherein R³⁸ is as defined hereinbefore in (9'));
- 13') C₁₋₅alkylX⁶R³⁸ (wherein X⁶ represents -O-, -S-, -SO-, -SO₂-, -NR⁴³CO-, -CONR⁴⁴-, -SO₂NR⁴⁵-, -NR⁴⁶SO₂- or -NR⁴⁷- (wherein R⁴³, R⁴⁴, R⁴⁵, R⁴⁶ and R⁴⁷ each independently represents hydrogen, C₁₋₃alkyl or C₁₋₃alkoxyC₂₋₃alkyl) and R³⁸ is as defined hereinbefore in (9'));
- 14') C₂₋₅alkenylX⁷R³⁸ (wherein X⁷ represents -O-, -S-, -SO-, -SO₂-, -NR⁴⁸CO-, -CONR⁴⁹-, -SO₂NR⁵⁰-, -NR⁵¹SO₂- or -NR⁵²- (wherein R⁴⁸, R⁴⁹, R⁵⁰, R⁵¹ and R⁵²

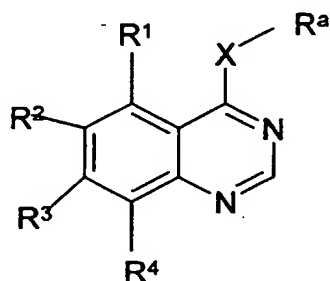
each independently represents hydrogen, C₁₋₃alkyl or C₁₋₃alkoxyC₂₋₃alkyl) and R³⁸ is as defined hereinbefore in (9'));

15') C₂₋₅alkynylX⁸R³⁸ (wherein X⁸ represents -O-, -S-, -SO-, -SO₂-, -NR⁵³CO-, -CONR⁵⁴-, -SO₂NR⁵⁵-, -NR⁵⁶SO₂- or -NR⁵⁷- (wherein R⁵³, R⁵⁴, R⁵⁵, R⁵⁶ and R⁵⁷ each independently represents hydrogen, C₁₋₃alkyl or C₁₋₃alkoxyC₂₋₃alkyl) and R³⁸ is as defined hereinbefore in (9'));

16') C₁₋₃alkylX⁹C₁₋₃alkylR³⁸ (wherein X⁹ represents -O-, -S-, -SO-, -SO₂-, -NR⁵⁸CO-, -CONR⁵⁹-, -SO₂NR⁶⁰-, -NR⁶¹SO₂- or -NR⁶²- (wherein R⁵⁸, R⁵⁹, R⁶⁰, R⁶¹ and R⁶² each independently represents hydrogen, C₁₋₃alkyl or C₁₋₃alkoxyC₂₋₃alkyl) and R³⁸ is as defined hereinbefore in (9'));

17') C₁₋₃alkylX⁹C₁₋₃alkylR³⁷ (wherein X⁹ and R³⁷ are as defined hereinbefore (in 5')) in the preparation of a medicament for use in the inhibition of aurora 2 kinase.

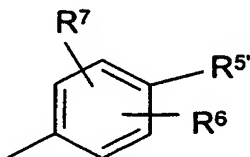
9. The use according to any one of claims 1 to 5 where the compound of formula (I) is a compound of formula (IV)



(IV)

or a salt, ester, amide or prodrug thereof;

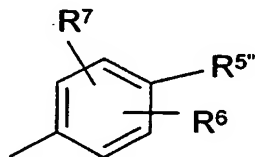
where R¹, R², R³, R⁴ and X are as defined in claim 1 and R^{a'} is a 3-quinoline group or a group of sub-formula (i)



(i)

where R⁶ and R⁷ are as defined in relation to formula (I) and R^{5''} is halogen or a group of formula NR¹⁰R^{10'} where R¹⁰ and R^{10'} are as defined in claim 1.

10. The use according to claim 9 wherein the compound of formula (VI) is a compound of formula (IVA) which is of structure (IV) as shown above, or a salt, ester or amide thereof;
- where X is O, or S, S(O) or S(O)₂, or NR⁸ where R⁸ is hydrogen or C₁₋₆alkyl; R^a is a 3-quinoline group or a group of sub-formula (i)



(i)

where R^{5''} is halogen or a group of formula NR¹⁰R^{10'} where R¹⁰ and R^{10'} are selected from hydrogen or optionally substituted hydrocarbyl or R¹⁰ and R^{10'} together with the nitrogen atom to which they are attached form a heterocyclic ring which may optionally contain further heteroatoms or an azo group of formula -N=N-R¹¹ where R¹¹ is an optionally substituted hydrocarbyl group or optionally substituted heterocyclic group;

R⁶ and R⁷ are independently selected from hydrogen, halo, C₁₋₄alkyl, C₁₋₄alkoxy, C₁₋₄alkoxymethyl, di(C₁₋₄alkoxy)methyl, C₁₋₄alkanoyl, trifluoromethyl, cyano, amino, C₂₋₅alkenyl, C₂₋₅alkynyl, a phenyl group, a benzyl group or a 5-6-membered heterocyclic group with 1-3 heteroatoms, selected independently from O, S and N, which heterocyclic group may be aromatic or non-aromatic and may be saturated (linked via a ring carbon or nitrogen atom) or unsaturated (linked via a ring carbon atom), and which phenyl, benzyl or heterocyclic group may bear on one or more ring carbon atoms up to 5 substituents selected from hydroxy, halogeno, C₁₋₃alkyl, C₁₋₃alkoxy, C₁₋₃alkanoyloxy, trifluoromethyl, cyano, amino, nitro, C₂₋₄alkanoyl, C₁₋₄alkanoylamino, C₁₋₄alkoxycarbonyl, C₁₋₄alkylsulphanyl, C₁₋₄alkylsulphinyl, C₁₋₄alkylsulphonyl, carbamoyl, N-C₁₋₄alkylcarbamoyl, N,N-di(C₁₋₄alkyl)carbamoyl, aminosulphonyl, N-C₁₋₄alkylaminosulphonyl, N,N-di(C₁₋₄alkyl)aminosulphonyl, C₁₋₄alkylsulphonylamino, and a saturated heterocyclic group selected from morpholino, thiomorpholino, pyrrolidinyl, piperazinyl, piperidinyl imidazolidinyl and pyrazolidinyl, which saturated heterocyclic group may bear 1 or 2

substituents selected from oxo, hydroxy, halogeno, C₁₋₃alkyl, C₁₋₃alkoxy, C₁₋₃alkanoyloxy, trifluoromethyl, cyano, amino, nitro and C₁₋₄alkoxycarbonyl, and

R¹, R², R³, R⁴ are independently selected from, halo, cyano, nitro, trifluoromethyl,

C₁₋₃alkyl, -NR¹²R¹³ (wherein R¹² and R¹⁴, which may be the same or different, each represents hydrogen or C₁₋₃alkyl), or -X¹R¹⁴ (wherein X¹ represents a direct bond, -O-, -CH₂-, -OCO-, carbonyl, -S-, -SO-, -SO₂-, -NR¹⁵CO-, -CONR¹⁶-, -SO₂NR¹⁷-, -NR¹⁸SO₂- or -NR¹⁹- (wherein R¹⁵, R¹⁶, R¹⁷, R¹⁸ and R¹⁹ each independently represents hydrogen, C₁₋₃alkyl or C₁₋₃alkoxyC₂₋₃alkyl), and R¹⁴ is selected from one of the following groups:

1') hydrogen or C₁₋₅alkyl which may be unsubstituted or which may be substituted with one or more groups selected from hydroxy, fluoro or amino,

2') C₁₋₅alkylX²COR²⁰ (wherein X² represents -O- or -NR²¹- (in which R²⁰ represents hydrogen, C₁₋₃alkyl or C₁₋₃alkoxyC₂₋₃alkyl) and R²¹ represents C₁₋₃alkyl, -NR²²R²³ or -OR²⁴ (wherein R²², R²³ and R²⁴ which may be the same or different each represents hydrogen, C₁₋₃alkyl or C₁₋₃alkoxyC₂₋₃alkyl);

3') C₁₋₅alkylX³R²⁵ (wherein X³ represents -O-, -S-, -SO-, -SO₂-, -OCO-, -NR²⁶CO-, -CONR²⁷-, -SO₂NR²⁸-, -NR²⁹SO₂- or -NR³⁰- (wherein R²⁶, R²⁷, R²⁸, R²⁹ and R³⁰ each independently represents hydrogen, C₁₋₃alkyl or C₁₋₃alkoxyC₂₋₃alkyl) and R²⁵ represents hydrogen, C₁₋₃alkyl, cyclopentyl, cyclohexyl or a 5-6-membered saturated heterocyclic group with 1-2

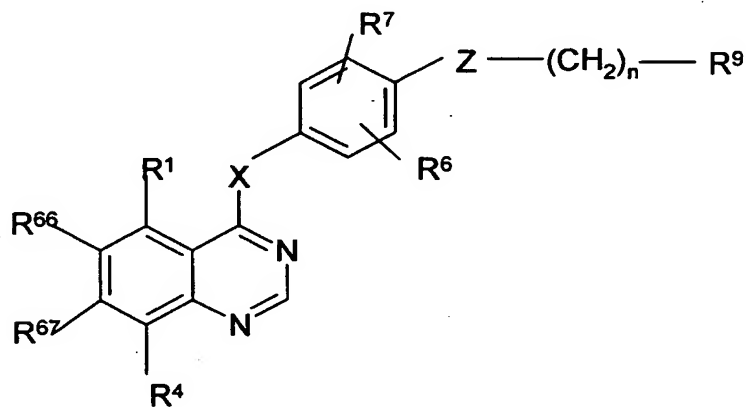
heteroatoms, selected independently from O, S and N, which C₁₋₃alkyl group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno and C₁₋₄alkoxy and which cyclic group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno, C₁₋₄alkyl, C₁₋₄hydroxyalkyl and C₁₋₄alkoxy);

4') C₁₋₅alkylX⁴C₁₋₅alkylX⁵R³¹ (wherein X⁴ and X⁵ which may be the same or different are each -O-, -S-, -SO-, -SO₂-, -NR³²CO-, -CONR³³-, -SO₂NR³⁴-, -NR³⁵SO₂- or -NR³⁶- (wherein R³², R³³, R³⁴, R³⁵ and R³⁶ each independently represents hydrogen, C₁₋₃alkyl or C₁₋₃alkoxyC₂₋₃alkyl) and R³¹ represents hydrogen or C₁₋₃alkyl);

- 5') R^{37} (wherein R^{37} is a 5-6-membered saturated heterocyclic group (linked via carbon or nitrogen) with 1-2 heteroatoms, selected independently from O, S and N, which heterocyclic group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno, C_{1-4} alkyl, C_{1-4} hydroxyalkyl, C_{1-4} alkoxy, C_{1-4} alkoxy C_{1-4} alkyl and C_{1-4} alkylsulphonyl C_{1-4} alkyl);
- 6') C_{1-5} alkyl R^{37} (wherein R^{37} is as defined hereinbefore in (5'));
- 7') C_{2-5} alkenyl R^{37} (wherein R^{37} is as defined hereinbefore in (5'));
- 8') C_{2-5} alkynyl R^{37} (wherein R^{37} is as defined hereinbefore in (5'));
- 9') R^{38} (wherein R^{38} represents a pyridone group, a phenyl group or a 5-6-membered aromatic heterocyclic group (linked via carbon or nitrogen) with 1-3 heteroatoms selected from O, N and S, which pyridone, phenyl or aromatic heterocyclic group may carry up to 5 substituents on an available carbon atom selected from hydroxy, halogeno, amino, C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} hydroxyalkyl, C_{1-4} aminoalkyl, C_{1-4} alkylamino, C_{1-4} hydroxyalkoxy, carboxy, trifluoromethyl, cyano, $-CONR^{39}R^{40}$ and $-NR^{41}COR^{42}$ (wherein R^{39} , R^{40} , R^{41} and R^{42} , which may be the same or different, each represents hydrogen, C_{1-4} alkyl or C_{1-3} alkoxy C_{2-3} alkyl);
- 10') C_{1-5} alkyl R^{38} (wherein R^{38} is as defined hereinbefore in (9'));
- 11') C_{2-5} alkenyl R^{38} (wherein R^{38} is as defined hereinbefore in (9'));
- 12') C_{2-5} alkynyl R^{38} (wherein R^{38} is as defined hereinbefore in (9'));
- 13') C_{1-5} alkyl X^6R^{38} (wherein X^6 represents $-O-$, $-S-$, $-SO-$, $-SO_2-$, $-NR^{43}CO-$, $-CONR^{44}-$, $-SO_2NR^{45}-$, $-NR^{46}SO_2-$ or $-NR^{47}-$ (wherein R^{43} , R^{44} , R^{45} , R^{46} and R^{47} each independently represents hydrogen, C_{1-3} alkyl or C_{1-3} alkoxy C_{2-3} alkyl) and R^{38} is as defined hereinbefore in (9'));
- 14') C_{2-5} alkenyl X^7R^{38} (wherein X^7 represents $-O-$, $-S-$, $-SO-$, $-SO_2-$, $-NR^{48}CO-$, $-CONR^{49}-$, $-SO_2NR^{50}-$, $-NR^{51}SO_2-$ or $-NR^{52}-$ (wherein R^{48} , R^{49} , R^{50} , R^{51} and R^{52} each independently represents hydrogen, C_{1-3} alkyl or C_{1-3} alkoxy C_{2-3} alkyl) and R^{38} is as defined hereinbefore in (9'));
- 15') C_{2-5} alkynyl X^8R^{38} (wherein X^8 represents $-O-$, $-S-$, $-SO-$, $-SO_2-$, $-NR^{53}CO-$, $-CONR^{54}-$, $-SO_2NR^{55}-$, $-NR^{56}SO_2-$ or $-NR^{57}-$ (wherein R^{53} , R^{54} , R^{55} , R^{56} and R^{57} each independently represents hydrogen, C_{1-3} alkyl or C_{1-3} alkoxy C_{2-3} alkyl) and R^{38} is as defined hereinbefore in (9'));

16') $C_{1-3}alkylX^9C_{1-3}alkylR^{38}$ (wherein X^9 represents -O-, -S-, -SO-, -SO₂-, -NR⁵⁸CO-, -CONR⁵⁹-, -SO₂NR⁶⁰-, -NR⁶¹SO₂- or -NR⁶²- (wherein R⁵⁸, R⁵⁹, R⁶⁰, R⁶¹ and R⁶² each independently represents hydrogen, C₁₋₃alkyl or C₁₋₃alkoxyC₂₋₃alkyl) and R³⁸ is as defined hereinbefore in (9')); and
 17') $C_{1-3}alkylX^9C_{1-3}alkylR^{37}$ (wherein X^9 and R³⁷ are as defined hereinbefore (in 5').

11. A compound of formula (IIB)



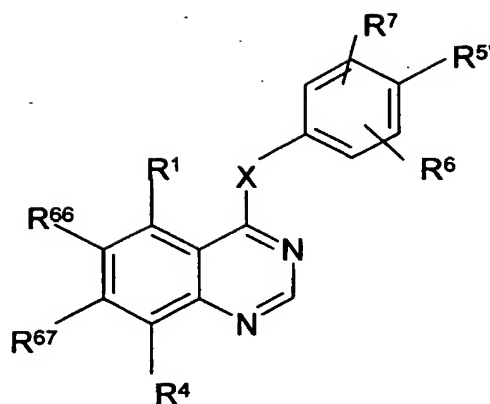
(IIB)

or a salt, ester, amide or prodrug thereof

where X, Z, R⁹, R⁶ and R⁷ and n are as defined in claim 1 and R⁶⁶ is halo, cyano, nitro, trifluoromethyl, C₁₋₃alkyl, -NR¹²R¹³ (wherein R¹² and R¹³, which may be the same or different, each represents hydrogen or C₁₋₃alkyl), or a group -X¹R¹⁴ where X¹ and R¹⁴ are as defined in claim 1 ;

and R⁶⁷ is C₁₋₆alkoxy optionally substituted by fluorine or a group X¹R³⁸ in which X¹ and R³⁸ are as defined in claim 1; provided that at least one of R⁶⁶ and R⁶⁷ is other than unsubstituted methoxy; or

a compound of formula (IIIB)

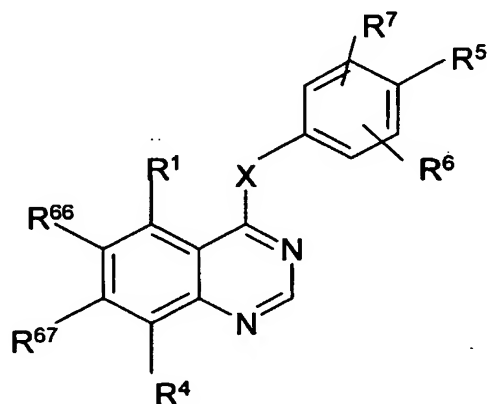


(IIIB)

or a salt, ester, amide or prodrug thereof,

where X, R⁴, R¹, R⁶ and R⁷ are as defined in claim 1 and R⁶⁶ and R⁶⁷ are as defined above and R^{5'} is as defined in claim 7: or

a compound of formula (IVB)

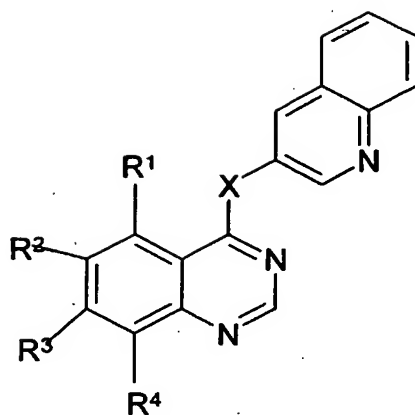


(IVB)

or a salt, ester, amide or prodrug thereof,

where X, R¹, R⁴, R⁶ and R⁷ and n are as defined in claim 1, R^{5''} is as defined in claim 9 and R⁶⁶ and R⁶⁷ are as defined above; or

a compound of formula (IVC)

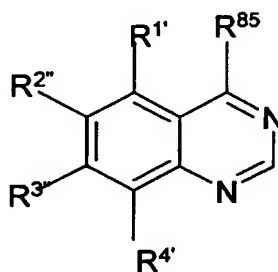


(IVC)

or a salt, ester, amide or prodrug thereof,

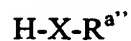
where R^1 , R^2 , R^3 , R^4 and X are as defined in claim 1.

12. A method of preparing a compound according to claim 11 which comprises reacting a compound of formula (VII)



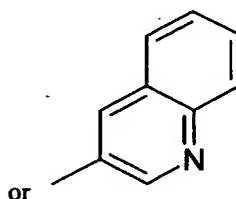
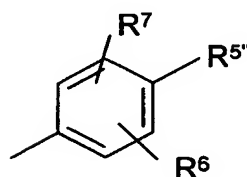
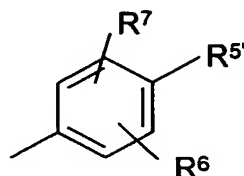
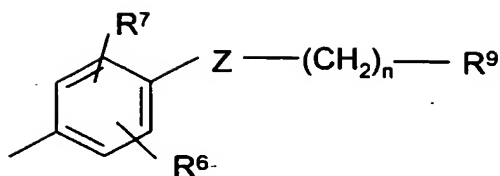
(VII)

where $R^{1'}$, $R^{2''}$, $R^{3'}$, and $R^{4'}$ are respectively equivalent to a group R^1 , R^{66} , R^{67} and R^4 as defined in claim 11 or a precursor thereof, and R^{85} is a leaving group, with a compound of formula (VIII)



(VIII)

where X, is as defined in claim 1, and $R^{a''}$ is selected from



where Z, n, R⁶, R⁷ and R⁹ are as defined in claim 1, R^{5'} is as defined in claim 7 and R^{5''} is as defined in claim 9;

and thereafter if desired or necessary converting a group R^{1'}, R^{2''}, R^{3''} or R^{4'} to a group R¹, R², R³ and R⁴ respectively or to a different such group.

13. A method for inhibiting aurora 2 kinase in a warm blooded animal, such as man, in need of such treatment, which comprises administering to said animal an effective amount of a compound of formula (I) as defined in claim 1, or a salt, ester, amide or prodrug thereof.
14. A compound of formula (IIB), (IIIB), (IVB) or (IVC) as defined in claim 11, or or a salt, ester, amide or prodrug thereof, for use in a method of treatment of the human or animal body by therapy.

15. A pharmaceutical composition comprising a compound of formula (IIB), (IIIB), (IVB) or (IVC) as defined in claim 11, or a salt, ester, amide or prodrug thereof, in combination with at pharmaceutically acceptable carrier.

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